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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,354	10/31/2001	Dennis M. Brown	A-70614/RFT/AMS	1942

7590 01/05/2004

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EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/996,354	BROWN, DENNIS M.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's amendment filed October 10, 2003 has been received and entered into the case. Claims 18 – 23 have been canceled. Claims 25 – 30 have been added, are pending and have been considered on the merits. All arguments have been fully considered.

Information Disclosure Statement

Applicant has requested that the Spanish-language document cited on the IDS filed March 10, 2003 and received on March 14, 2003 (document number C7) be considered, since applicant has provided a search report to a related PCT application, which cites the document and its relevance to the claims in the PCT application. However, the document will not be considered at this time since the statement of relevance is directed to claims that are different than the pending and examined claims in this application. Furthermore, it is noted that the instant application is not the national stage of the PCT, continuation or divisional of the PCT application, but claims benefit to the same provisional applications as the PCT application.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Frisch.

Applicant claims a composition comprising colchicines and cisplatin, wherein the modulation of a cellular proliferative disease by colchicines and cisplatin is greater that for colchicines or cisplatin alone.

Frisch teaches cisplatin and colchicines are chemotherapeutic agents which are used to treat cancer (col.4 line 46-55, claims).

Frisch does not specifically teach a composition comprising colchicine and cisplatin. However, at the time the claimed invention was made, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited reference above, since each is well known in the art for their claimed purpose. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine the instant ingredients with a reasonable expectation for successfully obtaining a composition that is more effective than each component alone. It is noted that such combination therapies were well known in the art at the time the claimed invention was made. In support, Abe (1999) teaches combination chemotherapies to include cisplatin (abstract), Earle (1999) teaches combination chemotherapies to include cisplatin (abstract) and Furue teaches general principles for combination chemotherapies (abstract). This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

3. Claims 25 – 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frisch and Bombardelli.

Applicant claims a composition comprising colchicines and cisplatin, wherein the modulation of a cellular proliferative disease by colchicines and cisplatin is greater that for colchicines or cisplatin alone. Applicant claims a composition comprising thiocolchicoside and cisplatin, wherein the modulation of a cellular proliferative disease by thiocolchicoside and cisplatin is greater that for thiocolchicoside or cisplatin alone. Applicant claims a composition comprising thiocolchicoside and camptothecin, wherein the modulation of a cellular proliferative disease by thiocolchicoside and camptothecin is greater that for thiocolchicoside or camptothecin alone. Applicant claims a composition comprising thiocolchicoside and etoposide, wherein the modulation of a cellular proliferative disease by thiocolchicoside and etoposide is greater that for thiocolchicoside or etoposide alone. Applicant claims a composition comprising thiocolchicoside and vinblastine, wherein the modulation of a cellular proliferative disease by thiocolchicoside and vinblastin is greater that for thiocolchicoside or vinblastine alone.

Frisch teaches etoposide, cisplatin, vinblastine, camptothecin and colchicines are chemotherapeutic agents that are used to treat cancer (col.4 line 46-55, claims).

Bombardelli teaches colchicine and its derivatives have antiproliferative and antineoplastice activities, which are cytotoxic to tumor cells (abstract). Specifically, thiocolchicoside is named to have these activities (col.1 line 18-29).

The references do not specifically teach a composition comprising the components together in a single composition. However, at the time the claimed invention was made, it would

have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited reference above, since each is well known in the art for their claimed purpose. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine the instant ingredients with a reasonable expectation for successfully obtaining a composition that is more effective than each component alone. It is noted that such combination therapies were well known in the art at the time the claimed invention was made. In support, Abe (1999) teaches combination chemotherapies to include cisplatin, etoposide and vinblastine (abstract), Earle (1999) teaches combination chemotherapies to include cisplatin and etoposide (abstract) and Furue teaches general principles for combination chemotherapies (abstract). This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

4. Claims 27 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bombardelli and Houghton.

Applicant claims a composition comprising thiocolchicoside and etoposide, wherein the modulation of a cellular proliferative disease by thiocolchicoside and etoposide is greater that for thiocolchicoside or etoposide alone. Applicant claims a composition comprising

thiocolchicoside and vinblastine, wherein the modulation of a cellular proliferative disease by thiocolchicoside and vinblastin is greater that for thiocolchicoside or vinblastine alone.

Bombardelli teaches colchicine and its derivatives have antiproliferative and antineoplastice activities, which are cytotoxic to tumor cells (abstract). Specifically, thiocolchicoside is named to have these activities (col.1 line 18-29).

Houghton teaches vinblastine, etoposide and colchicines are cytotoxic (claims 29 – 30) which are used to treat cancer (col.2 line 20-24).

The references do not specifically teach a composition comprising the components together in a single composition. However, at the time the claimed invention was made, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited reference above, since each is well known in the art for their claimed purpose. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine the instant ingredients with a reasonable expectation for successfully obtaining a composition that is more effective than each component alone. It is noted that such combination therapies were well known in the art at the time the claimed invention was made. In support, Abe (1999) teaches combination chemotherapies to include vinblastine and etoposide (abstract), Earle (1999) teaches combination chemotherapies to include etoposide (abstract) and Furue teaches general principles for combination chemotherapies (abstract). This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

5. Claims 27 – 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bombardelli and Ratain.

Applicant claims a composition comprising thiocolchicoside and etoposide, wherein the modulation of a cellular proliferative disease by thiocolchicoside and etoposide is greater that for thiocolchicoside or etoposide alone. Applicant claims a composition comprising thiocolchicoside and camptothecin, wherein the modulation of a cellular proliferative disease by thiocolchicoside and camptothecin is greater that for thiocolchicoside or camptothecin alone. Applicant claims a composition comprising thiocolchicoside and vinblastine, wherein the modulation of a cellular proliferative disease by thiocolchicoside and vinblastin is greater that for thiocolchicoside or vinblastine alone.

Bombardelli teaches colchicine and its derivatives have antiproliferative and antineoplastice activities, which are cytotoxic to tumor cells (abstract). Specifically, thiocolchicoside is named to have these activities (col.1 line 18-29).

Ratain teaches campothecin exhibits antitumor activity and is used to treat cancer (col.9 line 58 – col.10 line 10). Other antineoplastic compounds are named to include vinblastine, colchicines, etoposide (example 24).

The references do not specifically teach a composition comprising the components together in a single composition. However, at the time the claimed invention was made, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their

known benefit, as disclosed by the cited reference above, since each is well known in the art for their claimed purpose. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine the instant ingredients with a reasonable expectation for successfully obtaining a composition that is more effective than each component alone. It is noted that such combination therapies were well known in the art at the time the claimed invention was made. In support, Abe (1999) teaches combination chemotherapies to include etoposide and vinblastine (abstract), Earle (1999) teaches combination chemotherapies to include etoposide (abstract) and Furue teaches general principles for combination chemotherapies (abstract). This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

6. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bombardelli and Joseph.

Applicant claims a composition comprising thiocolchicoside and paclitaxel, wherein the modulation of a cellular proliferative disease by thiocolchicoside and paclitaxel is greater that for thiocolchicoside or paclitaxel alone.

Bombardelli teaches colchicine and its derivatives have antiproliferative and antineoplastice activities, which are cytotoxic to tumor cells (abstract). Specifically, thiocolchicoside is named to have these activities (col.1 line 18-29).

Joseph teaches paclitaxel is a chemotherapeutic drug used to treat cancer (abstrasct, col.2 line 24-29).

The references do not specifically teach a composition comprising the components together in a single composition. However, at the time the claimed invention was made, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited reference above, since each is well known in the art for their claimed purpose. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine the instant ingredients with a reasonable expectation for successfully obtaining a composition that is more effective than each component alone. It is noted that such combination therapies were well known in the art at the time the claimed invention was made. In support, Abe (1999) teaches combination chemotherapies (abstract), Earle (1999) teaches combination chemotherapies to include paclitaxel (abstract) and Furue teaches general principles for combination chemotherapies (abstract). This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman,* 1943 C.D. 518.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Applicant argues that the references do not teach the specific combinations of components together in a single composition and that evidence of synergy is not required to overcome the above rejections.

However, these arguments fail to persuade because as stated in the MPEP, 2143.02, obviousness requires only a reasonable expectation of success. As stated in the rejections, since each of the claimed components were well know to exhibit cytotoxicity to cells and have chemotherapeutic value, one of ordinary skill in the art would certainly have been motivated to combine the instant ingredients with a reasonable expectation for successfully obtaining a composition that is more effective than each component alone. In addition, it was well known in the art to combine chemotherapies as stated by Abe, Earle and Furue. Since applicant has not provided any arguments or evidence that the combinations of ingredients exhibit an unexpected advantage, benefit, or activity, the claims stand rejected.

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Effective January 20, 2004, any inquires should be made to Ruth Davis whose telephone number is 571-272-0915. The examiner's supervisor, Michael Wityshyn, can be reached at 571-272-0926.

Ruth A. Davis; rad
December 23, 2003.

LEON B. LANKFORD, JR.
PRIMARY EXAMINER